Please cancel claims 113 and 122.

Please add the following new claim:

123. (new) The composition of claim 111, wherein the second vector encodes constant regions of a receptor protein.

REMARKS

Attached hereto is an Appendix showing the changes made to the specification and the claims, as amended.

The Description of the Drawings for Figures 2 – 4 and 8 – 10 have been amended to insert "standard" identifiers to individual panels within each drawing. For example, "Figure 2" which had four panels, with the panels identified (a), (b), (c) and (d) has been explicitly amended to reflect "Figures 2A – 2D," confirming amendments have also been made. Thus, "(a)" has been replaced with "Figure 2A." These amendments are supported by the identifiers which were present in the original paragraph (e.g., "a"), and as such they do not introduce new matter. These amendments to the "Detailed Description of the Drawings" are also supported by reference to the individual panels of the drawings elsewhere in the specification. For example, the amendment to Figure 2A is supported at page 27, line 31 and page 28, line 1. The Amendment to Figure 2B is supported at page 27, line 26. The Amendment to Figure 2C is supported at page 29, line 2. The Amendment to Figure 2D is supported at page 29, line 26. The Amendment to Figure 3B is supported at page 35, line 6. The Amendment to Figure 3C is supported at page 35, line 16. The Amendment to Figure 4A is supported at page 36, line 3. The Amendment to Figure 4B is supported at page 36, line 11. The Amendment to Figure 4C is supported at page 35, line 25. The Amendment to Figure 8A is supported at page 40, line 21. The Amendment to Figure 8B is supported at page 40, line 30. The Amendment to Figure 9A is supported at page 41, line 6. The Amendment to Figure 9B is supported at page 41, line 9. The Amendment to Figure 10A is supported at page 49, line 8. The Amendment to Figure 10B is supported at page 49, line 2.

Claims 111 – 114 and 119 have been amended to expedite prosecution and make explicit that which was implicit. In particular, claims 111, 114, and 115 have been amended to replace "mass transfers" and "transferring in mass" with "in-mass transfer." These amendments are supported at page 17, line 30 through page 18, line 2; page 20, lines 9 – 20, page 26, lines 15 – 19; and page 34, lines 4 – 6. As such, these amendments do not constitute new matter and their entry is respectfully requested.

Claims 111, 112, and 114 have been amended to indicate that the library of fragments is inserted into a library of first vectors before their transfer to a library of second vectors. These amendments are supported at page 12, lines 14 – 18. These amendments do not introduce new matter, and their entry is respectfully requested.

Claims 111 and 121 have been amended with the phrase to "a polyclonal library of vectors or fragments thereof" instead of "polyclonal recombinant DNA molecules." Claim 120, which depends on claim 111, has been amended to conform to the amendment to claim 111. These amendments are supported at page 1, lines 8 – 12.

New claim 123 has been added to specify that in one preferred embodiment, the second vector encodes a constant region of a receptor protein. Support for this amendment can be found at page 24, lines 10 – 12. Claim 119, which is in part directed to constant regions, has been amended to depend on claim 123. These amendments do not introduce new matter and their entry is respectfully requested. Applicant appreciates the Examiner's statement that the claims are free of the prior art.

The drawings were objected to as failing to comply with 37 CFR 1.84(p)(5), because they include reference signs not mentioned in the description. Applicant respectfully submits that the figure identifiers were supported. However, the amendments to the specification, to use the same identifiers used in the drawings, have obviated this objection. Applicant respectfully points out that while not ipsis verbis how the identifiers used in the Description of the Drawings did correspond to the individual panels of the Drawings. For example, it is clear that the identifier "(a)" used in the description of "Figure 2" refers to Figure 2A in the drawings. Furthermore, the specification does use identifiers such as "Figure 2A" in the detailed description, for example at page 27, line 31 and page 28, line 1. Other examples of the explicit use of identifiers in the specification are provided above, as support for these amendments. Accordingly, applicant respectfully requests withdrawal of this objection.

Claims 111 – 122 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the invention.

Applicant respectfully submits that this rejection be withdrawn for the following reasons.

The Examiner has objected to the use of the phrases "in mass" and "transferring in mass" in claims 111, 114, and 115. Applicant respectfully submits that the amendments to these claims have obviated this objection.

While the Examiner contends that "in mass" and "transferring in mass" are indefinite because it is not clear how one would transfer the nucleic acid molecules and ensure they are transferred together, there is ample enablement throughout the specification to support this recitation. For example, the disclosure provides extensive guidance to a range of methods such as linking the genetic regions of the nucleic acid molecules encoding the variable regions, in order to ensure that are transferred together:

> "... yielding a population of DNA fragments which encode **the linked V_H and V_L genetic regions**... The grouping of V_H and V_L combinations is an advantage of this process **and allows for the in mass transfer** or batch transfer of all clones... [page 17, line 30 – page 18, line 2; emphasis added]

See also page 20, lines 9- 12. Furthermore, the specification exemplifies at page 17 how the linkage of the variable regions can be achieved with PCR amplification and hybridization of complementary terminal sequences. Accordingly, Applicant respectfully submits that the specification provides explicit detail regarding how to achieve the mass transfer of these fragments. Nevertheless, applicant has made an editorial change to the claims to expedite prosecution.

The Examiner has also taken the position that the use of "first vectors" is indefinite because it is unclear what is a first vector. Applicant respectfully submits that such language is understandable, but to expedite prosecution amended the claims. Those amendments to these claims have obviated this objection, as claim 111 now recites the use of a first vector followed by transfer into a second vector. More particularly, the second vectors are the product of the in-mass transfer from the library of first vectors into separate, second vectors, as described in detail at page 12, lines 14 – 18.

The Examiner has objected to the phrases "polyclonal recombinant DNA" and "polyclonal nucleic acid" in claims 111, 120, and 121. Applicant respectfully submits that the

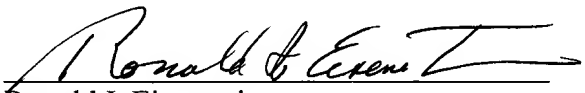
amendment of these claims, which replaces these phrases with "a polyclonal library of vectors or fragments thereof," has obviated this rejection. From the field of the invention and the specification, it would be clear to one skilled in the art that the phrase "a polyclonal library" means a collection of vectors comprising pairs of variable regions that are diverse from one another and thus provide for the polyclonality of the protein they encode. Accordingly, Applicant respectfully submits that this rejection should be withdrawn.

Accordingly, in view of the foregoing, Applicant respectfully submits that all claims comply with 35 U.S.C. § 112, second paragraph.

In view of the foregoing, Applicant submits that all claims are in condition for early and favorable allowance. Early and favorable action is requested.

Respectfully submitted,

Date: 3/3/03



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APPENDIX

The changes made by the amendments to the specification and the claims are shown below, with insertions being underlined and deletions being bracketed.

IN THE SPECIFICATION:

Please replace the paragraph on page 12, lines 25 – 26, with the following paragraph:

Figures 2A – 2D. [Figure 2.] Diagrammatic representation of the construction of (Figure 2A) [(a)] pUC19-Cκ-CH1, (Figure 2B) [(b)] pUC119-Cκ-CH1, (Figure 2C) [(c)] p*lPPl2*, and (Figure 2D) [(d)] pJS.

Please replace the paragraph bridging page 12, line 27 to page 13, line 1, with the following paragraph:

Figures 3A – 3C. [Figure 3.] Partial maps of phagemid expression vectors (Figure 3A) [(a)] pComb3, (Figure 3B) [(b)] phh3, (Figure 3C) [(c)] p*lPPl*, and (Figure 2D) [(d)] phh3mu or phh3hu, shown not to scale. Amino acids contributed by the vectors are shown in one letter code in front of the Fd and L chain genes. P = promoter; l – leader sequence; lmod = leader sequence with modified nucleotide sequence.

Please replace the paragraph on page 13, lines 2 – 6, with the following paragraph:

Figures 4a – 4C. [Figure 4.] Schematic diagram of (Figure 4A) [(a)] a murine dual vector, pMDV, (Figure 4B) [(b)] a chimeric dual vector, pCDV; wherein: P = promoter; E = enhancer; l = leader; ss = splice site; hum = human; and (Figure 4C) [(c)] the bulk transfer of variable region sequences between bacterial and mammalian vectors.

Please replace the paragraph on page 13, line 9, with the following paragraph:

Figures 8A – 8B. [Figure 8.] Cell supernatant analysis by (Figure 8A) [(a)] Western blot and (Figure 8B) [(b)] ELISA.

Please replace the paragraph on page 13, lines 10 – 11, with the following paragraph:

Figures 9A – 9B. [Figure 9.] Analysis of phage binding to Ars-BSA by (Figure 9A) [(a)] direct-binding ELISA, and (Figure 9B) [(b)] inhibition ELISA.

Please replace the paragraph on page 13, lines 12 – 14, with the following paragraph:

Figures 10A – 10B. [Figure 10.] Generation of (Figure 10A) [(a)] bacterial and (Figure 10B) [(b)] mammalian vectors for expression of Fab phage-display libraries or intact antibodies derived from head-to-head linked V_H-V_L combinations.

IN THE CLAIMS:

111. (amended) A composition comprising a polyclonal library of vectors or fragments thereof, [recombinant DNA molecules,] wherein each vector [DNA molecule] contains a nucleic acid segment that encodes a pair of variable regions capable of associating with each other to form a binding domain and, wherein the totality of nucleic acid segments provides the polyclonality of said library of vectors, and [comprises a library of polyclonal nucleic acid segments,] wherein said polyclonal library of vectors [polyclonal nucleic acid segments] has been obtained by inserting said nucleic acid segments into [transferred in mass from a library of] first vectors followed by in-mass transfer of said nucleic acid segments to second vectors.

112. (amended) The composition of claim 111 wherein [the vectors of] said [library of] first vectors are suitable for selection of nucleic acid segments encoding the variable region binding domains.

114. (amended) The composition of claim 111 wherein said [library of] first vector [vectors] has been selected from a larger library of vectors before said in-mass transfer, said larger library of vectors containing nucleic acid segments wherein each segment

encodes a pair of variable regions capable of associating with each other to form a binding domain.

115. (amended) The composition of claim 111 wherein the [transferring in mass] in-mass transfer is performed without characterization of all individual library members.

119. (amended) The composition of claim 123 [111] wherein said variable regions are derived from one species and constant regions are derived from another species.

120. (amended) The composition of claim 111 wherein said [polyclonal] nucleic acid segments are capable of expressing polyclonal receptor proteins wherein each receptor protein contains a pair of variable regions.

121. (amended) A composition comprising a polyclonal library of vectors or fragments thereof, [recombinant DNA molecules] wherein each vector [molecule] encodes a full length receptor protein and wherein each vector [molecule] contains a nucleic acid segment that encodes a pair of variable regions which constitutes a part of the full length receptor protein, [is contained in one of the receptor proteins] wherein the variable regions of each pair associate with each other to form a binding domain wherein the totality of nucleic acid segments are diverse forming a polyclonal library of vectors [polyclonal nucleic acid segments], wherein the polyclonal library of vectors [binding domain constitutes a part of the full-length receptor protein and wherein the vectors] encode full-length receptor proteins where the full-length polyclonal receptor proteins comprise both target-specific and cross-reactive receptor proteins.